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Listing's Plane Dependence on Alternating Fixation in a Strabismus Patient

BART J. M. MELIS,*‡ JOHAN R. M. CRUYSBERG,† JAN A. M. van GISBERGEN*‡

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Listing's law of the eye is one of the best studied findings in motor control, but its functional meaning is still incompletely understood and its status in neurological disorders and in strabismus is almost entirely unknown. We investigated the mechanisms underlying Listing's law and its possible clinical relevance. The dual magnetic search coil technique was used to record three-dimensional binocular eye movements in a stereoblind strabismic patient with good visual acuity in both eyes and capable of voluntarily alternating fixation. This technique yielded an accurate, objective and simultaneous measure of ocular misalignment in three dimensions and showed that the squint angle depended on which eye was fixating. Saccadic eye movement data throughout the oculomotor range were used to fit Listing's plane. Listing's primary position and the thickness of the plane for each eye were calculated for three different fixation conditions. For comparison, control measurements were taken from four normals. In the patient, no large deviations from normal values for the thickness of Listing's plane and the confidence limits of the Listing primary position were found. The most remarkable abnormality was that the orientation of Listing's plane depended on which eye was fixating. Both the change in ocular misalignment and the shift of Listing's primary positions observed when changing fixation are probably linked to accommodation-related vergence. Despite repeated surgery at early age, the patient had well-defined Listing planes for both eyes, but their alignment during left-eye fixation was abnormal. The obedience to Listing's law may reflect a strategy which minimizes muscular effort in each eye separately. The abnormal fixation-condition dependence is probably due to an aberrant coupling with vergence. © 1997 Published by Elsevier Science Ltd. All rights reserved.

Saccadic eye movements Strabismus Listing's law Binocular vision Alternating fixation

INTRODUCTION

From the geometry of the six extra-ocular muscles one might be led to think that the eyes can be oriented freely in all three dimensions. However, when the subject is scanning a distant scene with the head stable and upright, the actual eye orientations appear to be severely restricted in torsion. This phenomenon is described by Listing's law, which states that if one expresses eye positions as rotation vectors (Haustein, 1989) or any similar vector representation, these eye position vectors are confined to a single head-fixed plane, called *Listing's plane* (e.g. Von Helmholtz, 1867). It has been established that Listing's law holds for fixations, smooth pursuit (Tweed *et al.*, 1992) and saccades (Tweed & Vilis, 1990; Minken *et al.*,

1993), but there are indications that it breaks down during sleep (Nakayama, 1975; Suzuki *et al.*, 1995). The question why the eyes show this restricted behaviour has intrigued investigators from a variety of fields for over a century. This is understandable because the answer may have important implications for the neurological and biomechanical organization of the oculomotor system. Due to the development of accurate three-dimensional eye movement recording techniques, a vast amount of relevant data on this topic has become available in the last few years. This work has shown that in near vision (Mok *et al.*, 1992; Van Rijn & Van den Berg, 1993; Minken & Van Gisbergen, 1994) and during body tilt (Haslwanter *et al.*, 1992) various small but consistent variations on Listing's law occur. It is often assumed that there is a biological purpose behind these phenomena, making it essential for the system to control eye position accurately in three-dimensions, both statically and dynamically. Some of the most intriguing questions are whether the neural control mechanism behind this reduction in degrees of freedom is intrinsically two- or three-dimensional in nature and what role biomechanical factors, such as the muscles and the tissues surrounding

*Department of Medical Physics and Biophysics, University of Nijmegen, P.O. Box 9101, NL-6500 HB Nijmegen, The Netherlands.

†Department of Ophthalmology, University Hospital Nijmegen St Radboud, P.O. Box 9101, NL-6500 HB Nijmegen, The Netherlands.

‡All correspondence should be addressed to Bart J. M. Melis and reprint requests to Jan van Gisbergen.

the eye, play in preventing major torsional excursion and keeping the eye in Listing's plane.

One possible point of view on the organization of Listing's law holds that during active vision the position of both eyes is neurally controlled in all three dimensions [for review, see e.g. Tweed & Vilis (1990); Crawford & Vilis (1995)] which makes it possible that Listing's law is even obeyed during fast movements. This raises the question of what the advantage of this Listing behaviour might be. In this connection, it has been suggested that Listing's law may serve a visual purpose, like optimizing the correspondence of the images in both eyes, or may underlie a motor strategy, such as minimizing muscle effort or eye eccentricity. From the failure to generate local deviations from Listing's law in an attempt to adapt the torsional position of the eye by persistent intra-saccadic rotation of the complete visual scene, Melis and Van Gisbergen (1995) concluded that Listing's law probably does not have a purely visual function. On the other hand, a pure motor purpose is equally unlikely, since this cannot readily explain the consistent changes found during vergence (e.g. Mok *et al.*, 1992) and body tilt (Haslwanter *et al.*, 1992). Recent modelling by Tweed (1994) suggests that Listing's law can be explained by combining the visual purpose of optimizing the correspondence of binocular images in the plane of regard and the motor purpose of minimizing eye eccentricity. This view implies that Listing's law is a neurally implemented strategy which steers the middle course between optimal visual and motor benefits. According to models of this type the mechanical properties of the plant are important in the sense that they determine what neural commands are needed to minimize eccentricity, or to achieve any kinematic end.

An alternative point of view posits that the brain makes no special effort to constrain the torsional position of the eye to Listing's plane during saccades (Schnabolk & Raphan, 1994). In this model the eyes are driven by a two-dimensional movement command in the pitch-yaw plane. A first version of this model predicted correct eye

positions during fixation, but yielded far too large deviations of Listing's law during saccades (Tweed *et al.*, 1994). However, the possibility that soft muscle pulleys (Demer *et al.*, 1995) could limit the freedom of movement of the eye in the torsional direction, has revived interest in this viewpoint. According to this hypothesis, Listing's law itself may still serve a useful purpose, but its implementation would partly reflect certain subtle biomechanical properties of the plant.

So far, research into this field has been mainly purely scientific in nature and little is known about the possible clinical applications of three-dimensional studies [see, however, Nakayama (1975), (1983); Van den Berg *et al.* (1995)]. Yet, investigation of patient oculomotor abnormalities might reveal important information of mutual interest. For instance, from the above formulated viewpoints on the mechanisms behind Listing's law, the question could be raised whether the eyes of a strabismic patient, whose eye muscles have been operated on, would still obey Listing's law. In this paper we aim at a better understanding of the possible mechanisms underlying Listing's law and its possible clinical applications by studying three-dimensional eye movements in such a patient. In his early years this patient had surgery on both eyes to correct strabismus of the left eye. Now he has good visual acuity in both eyes and can address each eye at will. However, he lacks stereoscopic vision and the amplitude of the significant residual ocular misalignment depends on which eye is fixating. Therefore, this patient, who volunteered to participate in a large number of experiments, seemed eminently suited to investigate whether changes in squint angle and possible aberrations in Listing behaviour may be related.

METHODS

Subjects

One 24-yr-old strabismus patient (SP) and four control subjects (denoted hereafter as S1–S4), aged between 23 and 33, participated in our experiments and gave

TABLE 1. Ophthalmological test results of patient SP

Situation	Maddox			Amblyoscope		Visual acuity	
	Age	Conv.	R/L	Conv.	R/L	R	L
First test	2	+23					
Second test	2	+25					
Third test	4	+23	15	+25	18		
Before first operation	4	+22	12	+33	19	1.0	0.8
After first operation	4	+4	5	+10	16		
Before second operation	5	+2	11	+8	19		
After second operation	5	0	4	+5	11		
Final test	10	0	8	+3	15	1.0	0.8
Right eye fixation	24	0	10	−3	13	1.2	0.9
Left eye fixation				0	17		

Visual acuity and ocular misalignment angles in degrees for left eye (except on bottom line where the values for the right eye are given during left fixation) as measured with the Maddox test and the major amblyoscope. Information taken from clinical status reports of SP. Abbreviations: R, right eye; L, left eye; Conv., convergence.

informed consent after the nature of the experiment had been explained. All controls had normal vision in both eyes and none of them showed any oculomotor deficit. Only S2 needed optical correction and wore contact lenses during the experiment.

In the patient, frequent ocular misalignment was first noticed at about 10 months after birth. His congenital strabismus later developed into a manifest esotropia of the left eye. According to a major amblyoscope test the horizontal deviation was 25 deg (convergence) and the right eye was 18 deg above the left eye. In the following such a deviation will be denoted as: +25 deg, 18 deg R/L. To allow normal development of vision in both eyes, the dominant right eye was patched for several hours a day over a period of *ca* 2 yr, starting at the age of two. The patient has been operated twice to correct for the esotropia (see Table 1). The first operation, at the age of 4 yrs, involved anterior transposition of the inferior oblique muscle in the right eye and recession of the medial rectus muscles of both eyes. A year later the residual misalignment was further reduced by a recession of the inferior rectus muscle of the left eye. At present, the patient has normal visual acuity in both eyes (right eye: 1.2; left eye: 0.9) with an uncorrected unilateral hypermetropia of the left eye of +1.75 D in far vision. He has no binocular vision at all (suppression zone ≥ 35 deg) and his ocular misalignment, according to clinical tests, is especially pronounced in the vertical direction (right-eye fixation: -3 deg, 13 deg R/L and left-eye fixation: 0 deg, 17 deg R/L).

Experimental procedure

During the experiment the subject was seated in a dimly lit room in front of a large tangent screen. The head was firmly stabilized in a comfortable upright position by a bite board and the subject was emphatically instructed not to blink during a trial.

Eye position was measured binocularly using the scleral three-dimensional-coil technique in two alternating perpendicular magnetic fields (Ferman *et al.*, 1987). The coil signals were amplified and demodulated in lock-in amplifiers (PAR 128 A). After that, they were low-pass filtered (-3 dB at 200 Hz; fourth order Bessel filter) and finally sampled with 12 bit resolution at a rate of 500 Hz/channel and stored for off-line analysis on the disk of a SUN-3/140 workstation.

Raw eye position signals were calibrated using the procedure described by Hess *et al.* (1992). Before the experimental session, the sensitivity of the coils was measured using a gimbal system. In the course of the experiment, several *in situ* calibrations were performed to determine the orientation of each eye coil, when the subject monocularly fixated the reference position, which was chosen to be straight-ahead, with the corresponding eye. To describe three-dimensional eye positions as rotations from this reference position, to the current position, a head-fixed coordinate system was used. The *x*-axis of this Cartesian, right-handed coordinate system pointed forward, the *y*-axis leftward and the *z*-axis

upward. Each eye position could now be described by a rotation vector \vec{r} .

$$\vec{r} = (r_x, r_y, r_z) = \tan\left(\frac{\rho}{2}\right) \cdot \vec{n} \quad (1)$$

in which \vec{n} is a unit vector denoting the orientation of the rotation axis and ρ is the amount of rotation about this axis (Haustein, 1989). Torsional eye position is described by the *x*-component of this rotation vector, while horizontal and vertical eye positions are specified by the *z*- and the *y*-component, respectively. All data could be expressed in degrees by using the inverse of Eq. (1). In this way, each vector yields the virtual rotation from the reference position to the instantaneous eye position. The trajectory of an eye during a movement is described by a sequence of these orientations, each with its own rotation vector.

A regular pattern of target positions was used, which consisted of either a fixed set of markers or a small light spot (0.8 deg dia). Both were presented on a screen at 1–1.8 m in front of the subject within a 35 deg range around the straight-ahead direction. Each trial started with fixation of a target straight-ahead. The subject was instructed to make radial saccades between this starting position and the eccentric targets and to fixate them carefully. In each session, separate recordings were taken to collect data for left-eye, right-eye and binocular fixation (the latter only in the controls). Patient SP had to fixate all targets in a particular experiment with only one eye. These experiments were repeated up to six times per session and each subject was tested on two or three separate days.

Data analysis

The velocity of the eye movements was calculated by differentiation of the position signals in half overlapping steps of 4 msec. After filtering with a 33 points, 75 Hz low-pass digital filter, the resulting velocity signal was used for automatic saccade detection which was checked by visual inspection. Incorrect trials were excluded from analysis. The data were inspected for the presence of long-term slow torsional drift due to coil slippage by comparing eye positions at the beginning of successive trials, throughout the experiment. All sections in which drift was suspected were excluded from analysis.

If Listing's law holds perfectly, the pooled eye positions of all possible viewing directions of one eye are confined to a single flat plane, called *Listing's plane*. During far vision in normal upright subjects the plane of each eye is fixed in the head and almost fronto-parallel. To test the validity of Listing's law, we used linear regression to fit our eye position data (at least 30 000 data points per experiment from both saccades and fixations) to a plane:

$$r_1 = a_1 + a_2 r_2 + a_3 r_3 \quad (2)$$

in which r_1 , r_2 , and r_3 are the torsional, vertical and horizontal components of the rotation vector, respectively [see Eq. (1)]. The parameter a_1 is the offset of the plane in the torsional direction but has no functional

meaning in the context of this paper. The precise orientation of the plane is uniquely determined by its perpendicular, which is called the *Listing primary gaze direction*. This direction is fully determined by the parameters a_2 and a_3 . The corresponding eye position is called *Listing primary position*. Although its direction is usually almost parallel to the x -axis, this primary position should not be confused with the clinical term denoting the straight-ahead direction.

A commonly used measure for the goodness of fit is the thickness of the plane, which is defined as the standard deviation of the perpendicular distance from all individual data points to the best fit plane (in degrees). In other words, the better the fit, the thinner the plane. To estimate the uncertainty in the fitted Listing primary position, given the noise in the data, its 95% confidence limits were determined based on the a_2 and a_3 fit results. The upper and lower limits, as determined with the statistical software package SPSS, are plotted in Fig. 5.

RESULTS

Fitting Listing's plane

The first obvious question to ask is whether the patient showed Listing-like behaviour in both eyes. According to Listing's law, a good description of three-dimensional eye orientation can be obtained by fitting far vision eye position data to a flat plane. In Fig. 1 the front and side view of the Listing's planes of both eyes are shown in magnetic field coordinates during right eye fixation. The commonly used measure for how accurately Listing's law holds is the thickness of this plane (see Methods section). Figure 2 depicts the mean thickness values for both eyes of all subjects in the three different fixation conditions. The measured thickness was of the same order for all controls (0.69 ± 0.19 deg, total average for S1–S4) and in each of the normals it was similar in both eyes. It is important in the context of this paper to note that no significant dependence on fixation condition was found. Accordingly, the mean values of the thickness of

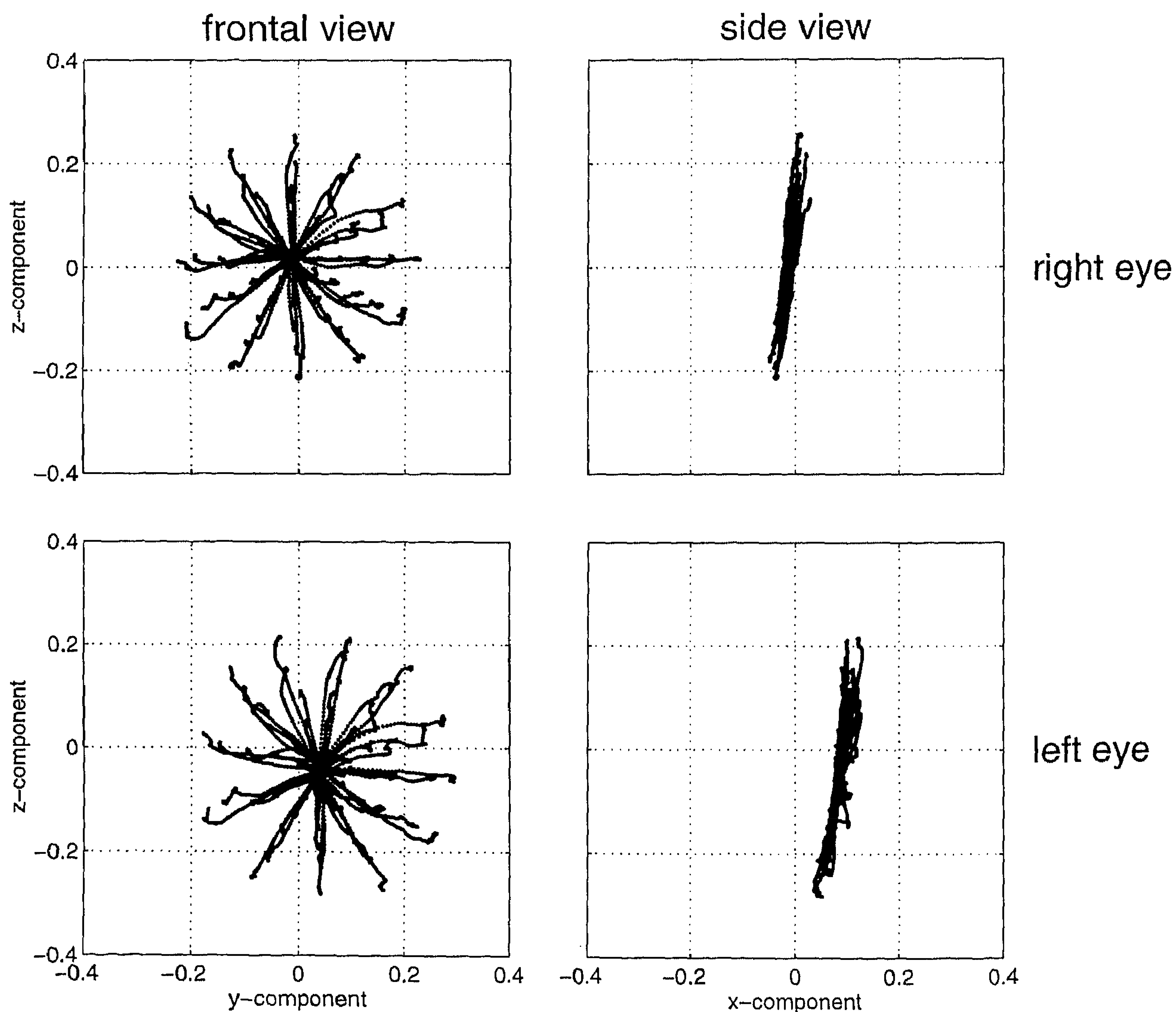


FIGURE 1. Front and side views of the Listing's planes of both eyes in patient SP during right eye fixation. All sampled eye positions are confined to a thin plane. Data in rotation vector units in magnetic-field coordinates (0.1 corresponds to *ca* 10 deg).

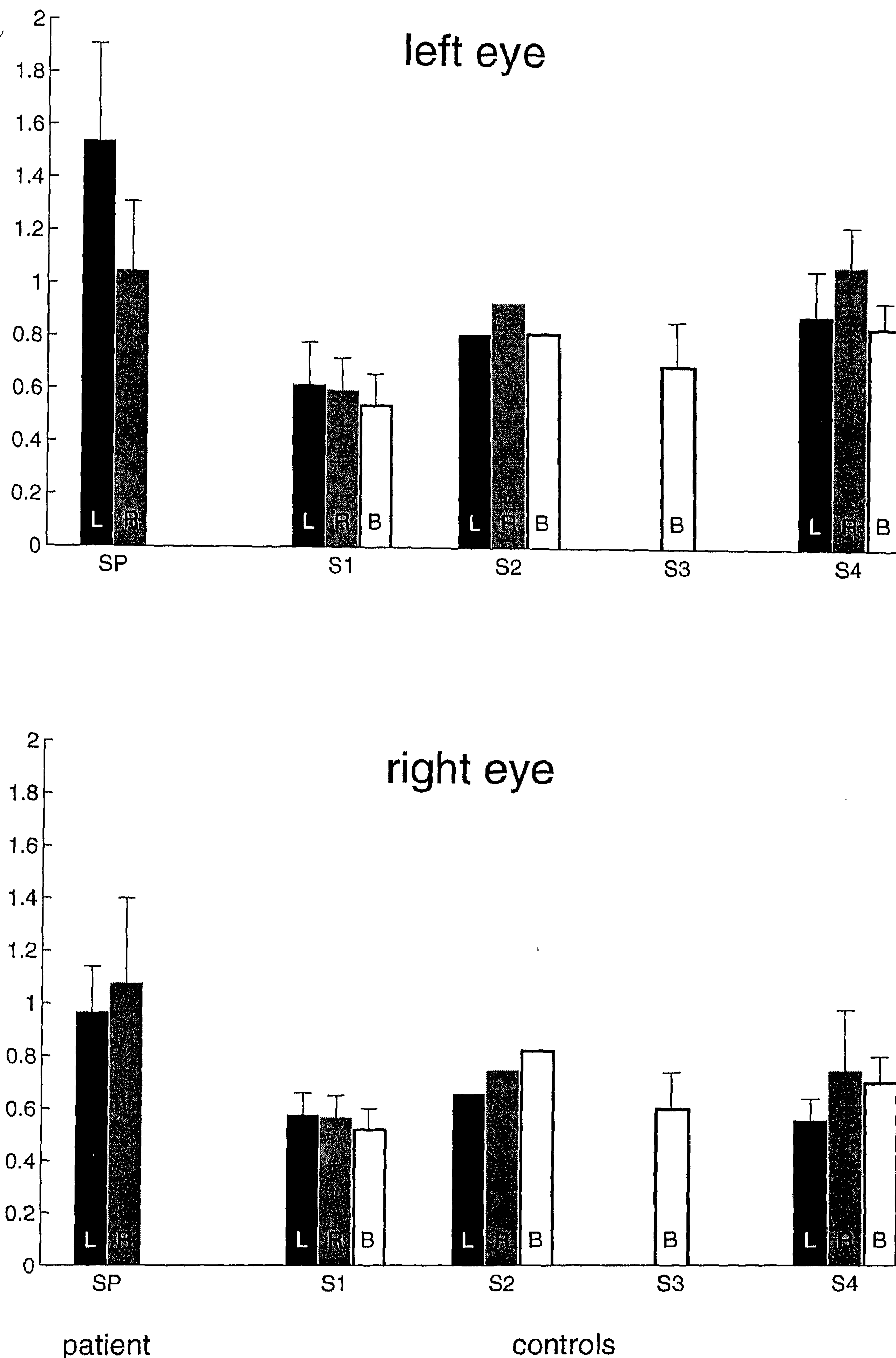


FIGURE 2. Thickness of the fitted planes for both eyes of all subjects in different fixation conditions. Bars denote mean and SD. Left eye fixation (L); right eye fixation (R); binocular fixation (B). Note that a significant dependence on fixation condition was found only in the left eye of patient SP.

the planes for the controls, as listed in Table 2, were obtained by averaging over all fixation conditions. As shown in Fig. 2, the average thickness of the planes in the patient and its variation between experiments was

significantly larger than in the controls. As in the controls, for the right, dominant eye there was no significant change in thickness with fixation condition (1.03 ± 0.25 deg). However, when fixation was changed

TABLE 2. Thickness data

Subject	Fixation	Left eye		Right eye	
		<i>N</i>	Thickness (deg)	<i>N</i>	Thickness (deg)
SP	Left	6	1.54 ± 0.37	6	1.05 ± 0.26
	Right	6	0.97 ± 0.17	6	1.08 ± 0.32
S1	Pooled	6	0.59 ± 0.11	6	0.56 ± 0.18
S2	Pooled	3	0.86 ± 0.07	3	0.78 ± 0.09
S3	Pooled	12	0.70 ± 0.13	12	0.60 ± 0.14
S4	Pooled	10	0.91 ± 0.13	24	0.70 ± 0.15

Mean ± SD thickness of the fitted planes for both eyes of all subjects. *N*, number of experiments. Data from the controls have been pooled over all fixation conditions.

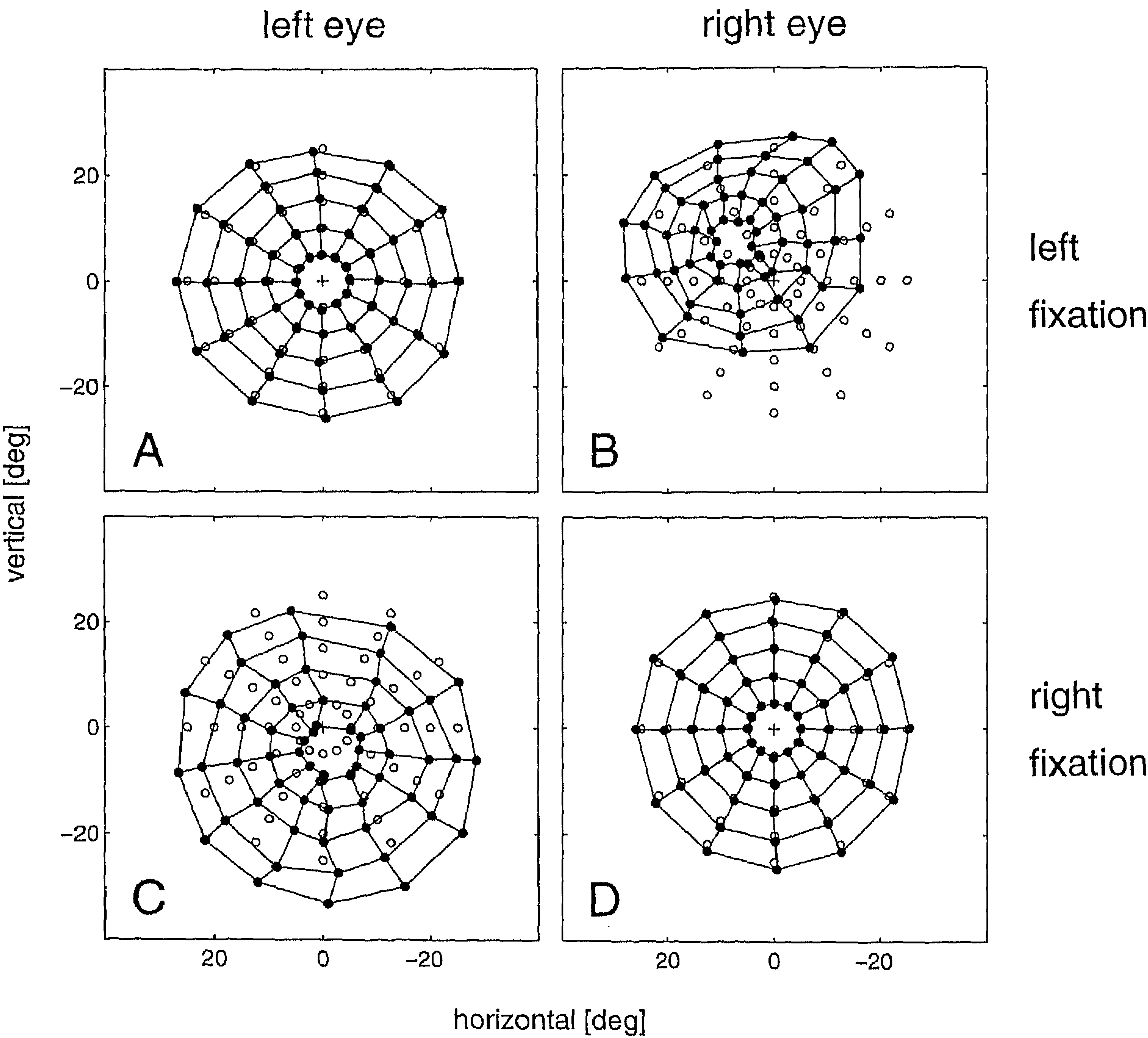


FIGURE 3. Deviation chart of patient SP. Targets (○) and fixation positions (●) for both eyes in the two fixation conditions. The cross indicates the straight-ahead position. Data as seen from behind the subject. (A) The left eye was nicely on target during left eye fixation. (B) In this condition, the right eye was obviously misaligned. When the left eye was directed straight-ahead, the right eye was looking 9.3 deg to the left and 8.3 deg upward. (C) Ocular misalignment was less severe during right eye fixation. When the right eye was directed straight-ahead, the left eye was looking 3.4 deg to the right and 3.9 deg downward. (D) The right eye was quite accurately on target during right eye fixation.

from the right eye to the left eye, the thickness of the left-eye plane increased significantly from 1.05 ± 0.26 deg to 1.54 ± 0.37 deg (two-sided *t*-test: $P < 0.05$). We fitted the data also to a second order model (similar to Radau *et al.* (1994)) but the resulting increase in the goodness of fit was too small to justify the additional number of parameters.

Squint angle

Since the dual magnetic search coil method is a very sensitive technique for measuring eye positions, the squint angle of the patient could be determined with high accuracy. Figure 3 shows a deviation chart for both eyes of SP in the different fixation conditions for a large number of target positions. The targets are depicted by open circles while the actual fixation positions are given by the filled symbols. To convey a better impression of the ocular misalignment pattern, the measured fixations have been interconnected by thin lines. For the fixating eye this yields a highly regular pattern of fixation positions, quite closely aligned with the targets [Fig. 3(A and D)]. By contrast, as is clear from Fig. 3(B and C), the fixation positions of the non-fixating eye deviate considerably from the target positions. As can be deduced from the shift of its fixation pattern, in most gaze directions the visual axis of the left eye pointed to the right and beneath the right eye, indicating a consistent convergent ocular misalignment (R/L). The mean squint angle for the left eye during straight-ahead fixation of the right eye was $+5.1 \pm 1.0$ deg, 4.7 ± 0.9 deg R/L ($n = 60$). From the fact that the pattern is mainly shifted and only slightly distorted [Fig. 3(C)] it can be concluded that this angle remained fairly constant for all viewing directions. Ocular misalignment was more severe for the right eye during straight-ahead fixation of the left eye ($+10.9 \pm 1.3$ deg, 8.1 ± 0.8 deg R/L; $n = 60$) and led to larger distortions in the periphery [Fig. 3(B)].

Listing's primary position of both eyes

So far, we have not discussed the orientation of the plane, which is fully characterized by its Listing primary position. For the controls, Listing's primary positions of both eyes and their 95% confidence intervals are depicted in Fig. 4. Although some day-to-day variation was observed (SD < 3 deg for all controls), they were always close to straight-ahead and in most cases reasonably aligned in the two eyes. Importantly, no consistent dependence on fixation condition was found.

For comparison, the Listing's primary positions of patient SP and their confidence intervals are depicted in Fig. 5. The 95% confidence areas are about the same size as in the normals, indicating once again that the planes in SP were well defined. During right eye fixation (marked R) the Listing's primary positions of both eyes were not markedly different from those in the controls (compare Fig. 4). For left eye fixation (marked L) they seemed somewhat abnormal in the sense that both lay left from the mid-sagittal plane and that the vertical misalignment was more severe. But the most striking abnormality in the

patient's behaviour was that the Listing's primary position of each eye changed depending on which eye was fixating. This shift accompanying alternating fixation is indicated by the lines, connecting two successive measurements with a different fixation condition, in Fig. 5. The Listing primary position of the left eye shifted on average 2.3 ± 1.0 deg to the right and 3.5 ± 1.6 deg upward when fixation changed from the left to the right eye. Although the same phenomenon of fixation-condition dependence occurred also consistently in the other eye, the direction of change in this case was different. As shown in the right-hand panel, the Listing's primary position of the right eye shifted almost purely horizontally (3.0 ± 0.7 deg to the left and 0.1 ± 0.7 deg downward) when fixation was changed from the right to the left eye. To rule out that the observed shift was caused by the fact that the oculomotor range for each eye varied with fixation condition (because of the ocular misalignment), a second set of planes was fitted using only the data points in the overlapping sections of the oculomotor ranges of both fixation conditions. The Listing primary positions determined from this second set differed < 1.5 deg from the accompanying Listing primary position in the original set and both showed a similar shift with fixation condition.

DISCUSSION

Validity of Listing's law

Since patient SP had undergone rather radical surgery on both eyes, it is not trivial that his three-dimensional eye position data would fit to a flat plane at all. Independent of whether neural factors or biomechanical mechanisms should be considered as most crucial in the implementation of Listing's law, deviations from the normally restricted behaviour are not a priori unlikely in these circumstances. After all, changes may have occurred at different levels, such as alteration of the transformation between the neural commands and the muscle response or changes in orbital tissues. Nevertheless, the calculated thicknesses of the sets of data points, used to test the validity of Listing's law (Fig. 2 and Table 2), suggest that the law holds in good approximation. Although the planes of SP were thicker than in the controls, all thickness values calculated from our experiments for both SP and the controls were still within the range for normal subjects reported in the literature. To illustrate, Tweed and Vilis (1990) found a mean thickness of 1.5 deg for combined fixations and saccades, whereas Straumann *et al.* (1991) and Haslwanter *et al.* (1994) reported 1.4 ± 0.5 deg and 0.8 ± 0.2 deg, respectively. Furthermore, both in the literature and in our data, the thickness of the planes was similar in both eyes. In none of the controls was a significant thickness dependence on fixation condition found, indicating that the accuracy to which Listing's law was obeyed did not change when the eye was covered. In SP this was only true for the dominant right eye. The thickness of the plane in his non-preferred left eye did

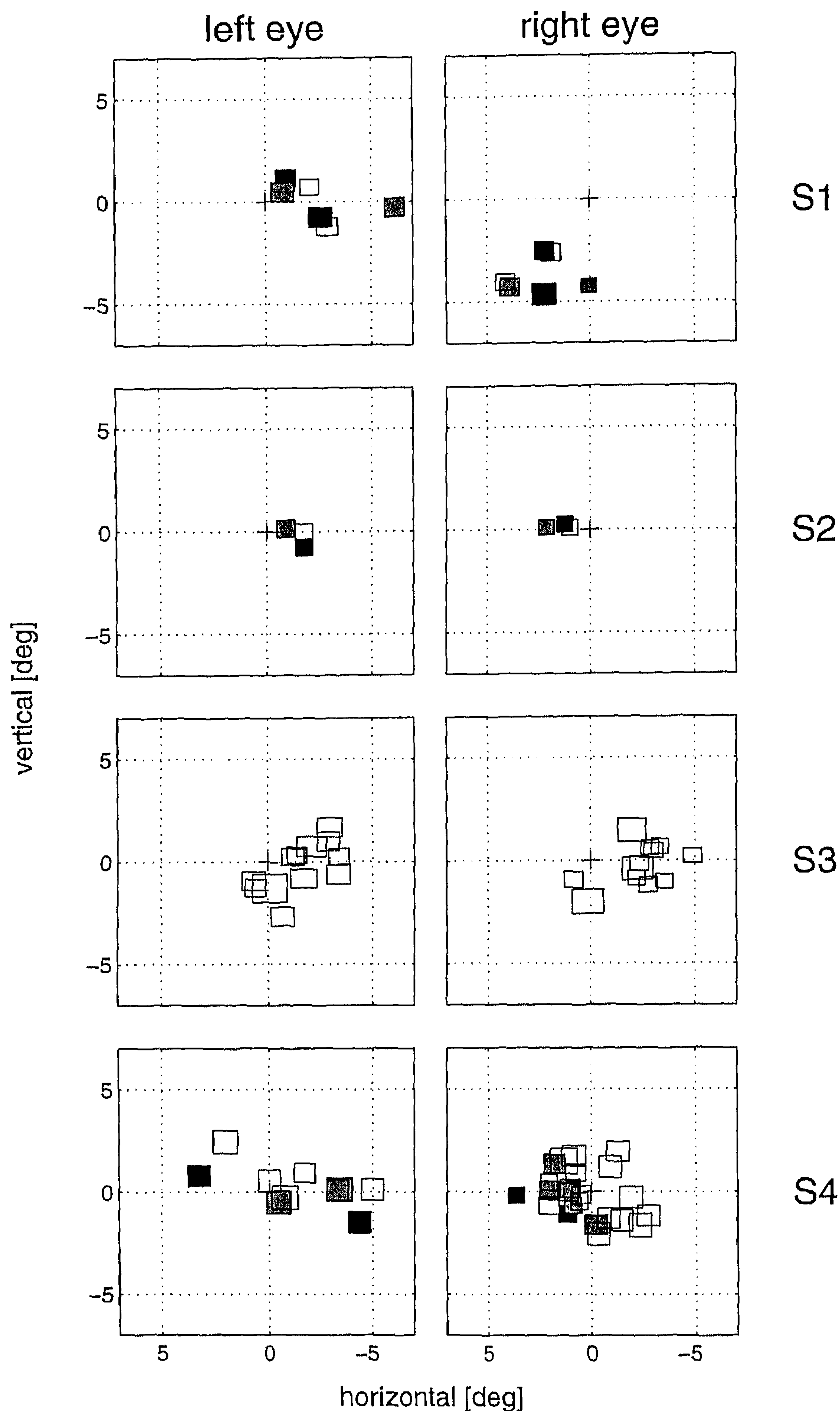


FIGURE 4. Listing primary positions in control subjects. The 95% confidence intervals of all Listing primary positions measured for both eyes are indicated by squares for the different fixation conditions: left eye fixation (black); right eye fixation (grey); binocular fixation (white). Data as seen from behind the subject. No dependence on fixation condition is apparent.

increase significantly when fixation was changed from the left eye to the right eye, which can be interpreted in a diminution of the accuracy to which Listing's law is obeyed. Nevertheless, these data suggest that the Listing planes of SP are fairly normal for all fixation conditions, despite the eye-muscle surgery in his early years and his lack of binocular vision.

From the literature not much is known about the behaviour of Listing's plane in strabismic patients and the consequences of eye surgery. In his Ph.D. thesis, Haustein (1988) described the planes of three patients before and after recession of one of the oblique muscles and reported that the operated eye still appeared to obey Listing's law in reasonable approximation in the sense

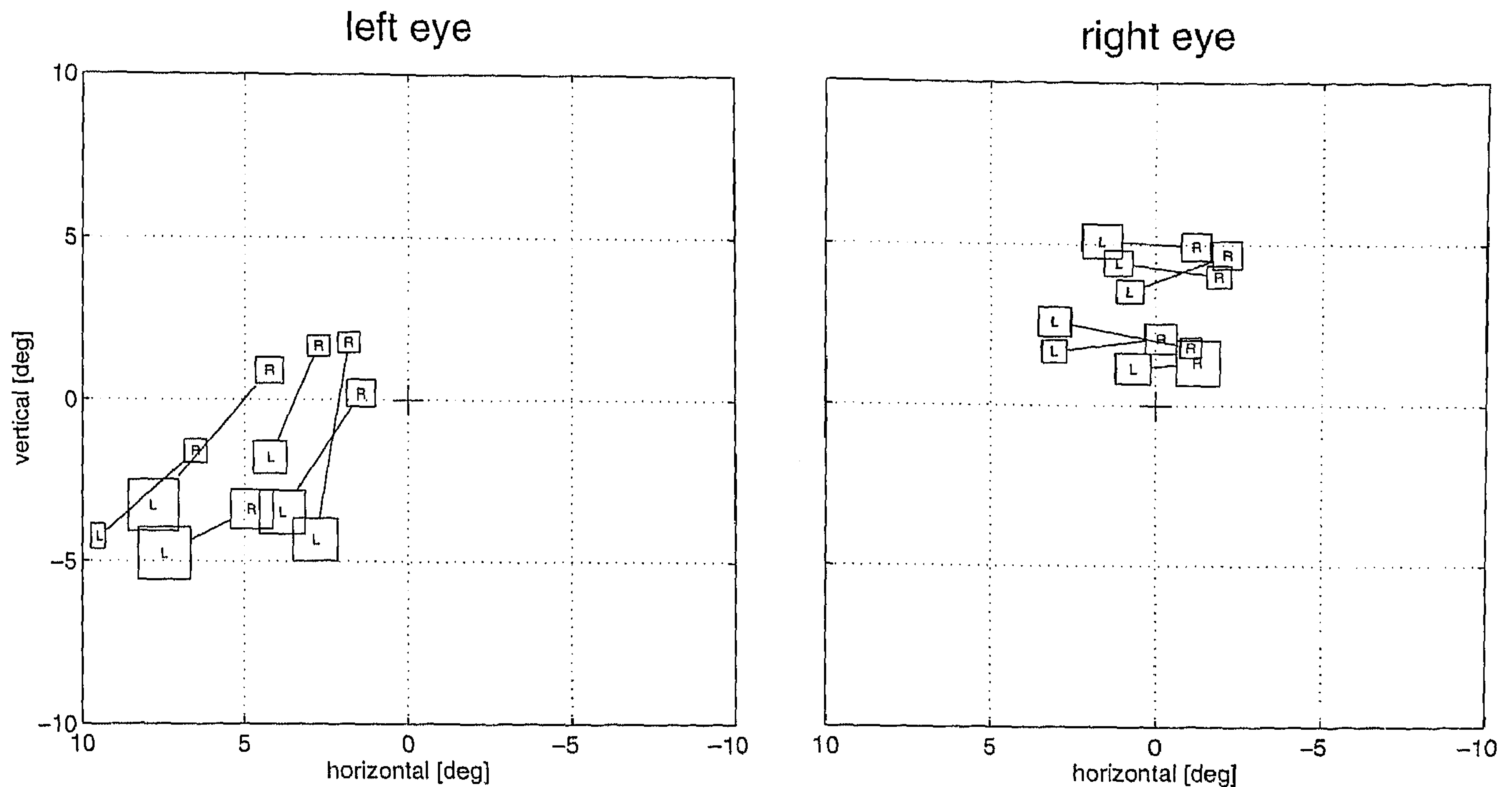


FIGURE 5. Shift of Listing's primary positions in patient SP upon alternating fixation. The 95% confidence intervals of all Listing's primary positions measured in both eyes are indicated by squares for both fixation conditions: left eye fixation (L); right eye fixation (R). Data as seen from behind the subject. Lines indicate the shift in Listing primary position after a change in fixation condition. In the left eye this shift is up and rightward, while it is mainly leftward in the right eye.

that the rotation vectors of eye position still lay in a single plane. Listing's primary position did change after surgery, but within a few weeks it moved back in its original direction, while that of the normal eye remained unchanged throughout the entire period. It remains unclear whether such a change of the Listing primary position in the operated eye is the result of a visual/neural adaptive feedback process, the reflection of a reorganization of muscle pulling directions or the consequence of orbital tissue recovery.

Clinical relevance

Most methods used to determine ocular misalignment in patients, like the major amblyoscope, the Maddox test and the Hess chart examination, yield subjective measures of the squint angle. These methods may yield varying results (Table 1 and Fig. 3) and have limited applicability in patients who lack binocular vision or have low visual acuity. The magnetic-dual search coil technique, on the other hand, is an objective method yielding accurate results, which can be used for tests in the dark, when the eyes are closed or covered and in both near and far vision. Consequently, it is a powerful tool to obtain an objective and absolute measure for the three-dimensional misalignment between the eyes in all viewing directions.

One of the interesting questions is whether the orientation of the Listing's planes of the two eyes is related to the ocular misalignment. As shown in Fig. 4, the orientation of Listing's plane in normals is subject to small day-to-day variations. Since the Listing primary positions of the two eyes are almost aligned, it has been

suggested that there is in fact a common binocular Listing's primary position (Van Rijn & Van den Berg, 1993; Minken & Van Gisbergen, 1994). Furthermore, no change with fixation condition was observed, so that the Listing's primary position of normals does not change when the eye is covered. The observed day-to-day variation in SP (see Fig. 5) was of the same order as in the controls, but a remarkable abnormality in this patient was that the Listing primary positions of the two eyes and their location relative to each other changed with fixation condition. For each experiment Fig. 6 shows the misalignment of the Listing primary positions of both eyes and the mean misalignment of the visual axes at the central fixation at the start of each trial. To facilitate comparison of the two fixation conditions, both are plotted for the left eye relative to the dominant right eye. While each of the two misalignments varied with fixation condition, they were obviously not identical. In other words, the difference between the Listing primary positions of both eyes is not simply a reflection of the misalignment of the visual axes.

Implications for Listing's law

We now come to discuss the possible mechanisms behind the observed shift in Listing's primary position. The reason behind this shift is not immediately obvious and its occurrence cannot be predicted easily from current viewpoints on the implementation and purpose of Listing's law.

Let us first consider the extreme view that Listing's law is purely the consequence of biomechanical factors without any neural basis. If this were the case, there

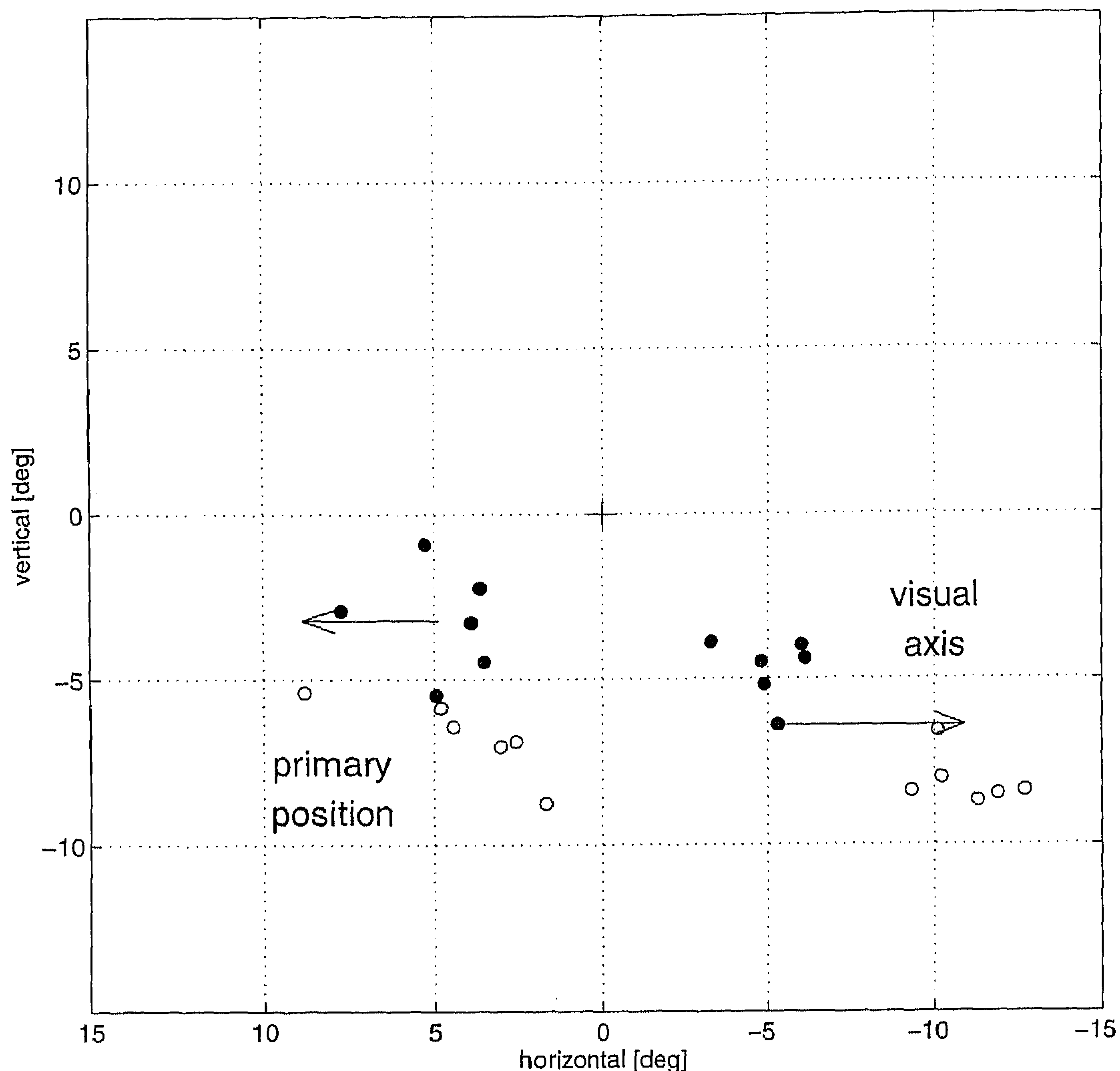


FIGURE 6. Misalignment of Listing's primary positions and of the visual axes of patient SP in both fixation conditions. Left-eye fixation (○); right-eye fixation (●). Data plotted with respect to the dominant right eye (crosshair). Each plotted symbol for the misalignment of the visual axis is the mean of the central fixations at the start of all trials during an experiment. Note that fixation with the non-dominant left eye causes increases in misalignment of both the visual axes and the Listing's primary positions of the two eyes. The leftward arrow denotes the change in Listing's primary position alignment predicted from the literature (4 deg) due to horizontal accommodative vergence change (6 deg, rightward arrow). The actual misalignment in Listing's primary position obviously does not change according to this prediction. Data as seen from behind the subject.

would be no reason why the torsional position of the eye should depend on which eye is fixating in such an orderly manner. The same holds for the above described viewpoint on the implementation of Listing's law (see Introduction), suggesting the possibility that the influence of the soft muscle pulleys (Demer *et al.*, 1995) prevents the eye from too large torsional deviations during saccades. Although there is a possibility that the pulleys are under smooth muscle control, it cannot be understood easily why their influence should change with fixation condition, so it is most likely that the observed variations reflect changes in the saccadic control signal. This idea is further strengthened by the findings that Listing's law can be violated during sleep (Nakayama, 1975; Suzuki *et al.*, 1995), that the orientation of the planes changes during body tilt (Haslwanter *et al.*, 1992) and that they rotate temporally during vergence (Mok *et al.*, 1992; Van Rijn & Van den Berg, 1993; Minken & Van Gisbergen, 1994). In fact, to the best of our knowledge, this temporal

rotation of Listing's plane with vergence angle and our finding of the shift in Listing's primary position with fixation condition in SP are the only currently known ways to modify Listing's law in upright subjects. To get a better feeling for what it really means to have a change in the orientation of Listing's plane, consider the left eye in Fig. 5 when its visual axis is pointing in a particular direction while the patient is fixating with the right eye and compare its torsional position when it is looking in the same direction during left eye fixation. Because the Listing primary position for the latter fixation condition is more downward, the rotation vector describing this position will be tilted further out of the yz-plane in most positions. Except for those viewing directions corresponding to the intersection of the two Listing planes, this results in more torsion although the viewing directions for the left eye are identical in both situations.

The shift of Listing's primary position with fixation condition and the fact that Listing's law remains valid

after surgery suggest that it has at least partially a neural basis. Tweed (1994) proposed that the purpose of this behaviour is to minimize a two-fold cost function, which implies both the motor goal of minimizing three-dimensional eye eccentricity from a resting position and the visual goal of maximizing the binocular correspondence of the plane of regard. Since patient SP is stereoblind, the presumed binocular advantage of Listing's law does not apply in his case and the cost function would reduce to minimizing the eccentricity of each eye from its resting position. Under these circumstances this theory is compatible with the existence of Listing's plane after surgery, perhaps due to some adaptive process, to minimize eccentricity. The existence of a small misalignment between the Listing primary positions of the two eyes might be due to the lack of binocular correcting mechanisms as well as to the fact that the optimal solution to the reduced cost function need not be the same for both eyes. So, in this light, it may not be surprising that the Listing planes of SP were not exactly aligned in far vision. However, since we cannot see how the resting position could change with fixation condition, the observed change of both Listing's primary positions with fixation condition can still not be explained by the strategy to minimize eccentricity.

Given the resemblance between our findings and phenomena observed during vergence in normals, the question arises whether the observed shift of Listing's primary position with fixation condition in SP may actually be the result of a horizontal vergence signal which is used in alternating foveation to the non-dominant eye. The existence of such a vergence component is plausible, because the unilateral hypermetropia of the left eye (see Methods section) causes an extra accommodation-related convergence input (near triad) upon the change of fixation from the right to the left eye. Figure 6 shows the ocular misalignment for both fixation conditions relative to the right eye, so it is automatically expressed in terms of vergence. Indeed, there appeared to be an additional disconjugate shift when changing from right eye to left eye fixation, with a horizontal component of about 6 deg convergence (rightward arrow). However, if the shift in Listing primary position were the consequence of the 6 deg vergence change during altering fixation, reports in the literature on normal subjects would predict a temporal rotation of Listing's plane (leftward arrow), whereas we found a downward change. Closer examination shows no relation between the horizontal component of the shift in Listing's primary position and the horizontal change in ocular misalignment ($n = 12$, $R = 0.51$, $P = 0.26$). By contrast, the vertical component of the Listing's primary position shift does depend significantly on the horizontal increase in ocular misalignment ($n = 12$, $R = 0.73$, $P < 0.01$). So, although there is actually a relation between the vergence component and the relative locations of the Listing primary positions in the two eyes, it does not simply follow the rules established in normal subjects. Since the change in Listing's primary position was only linked to

the horizontal change in vergence, the fact that a vertical shift in the orientation of Listing's plane in upright normals can also be induced by prism-induced vertical vergence (Mikhael *et al.*, 1995), does not seem relevant in the present context.

In summary, Tweed's theory of the two-fold cost function seems compatible with our findings that the patient does have Listing planes in the first place and that they are not aligned in the two eyes. Although the change in misalignment of the Listing primary position with fixation condition in SP was not exactly as might be expected from the literature on Listing's law in near vision, it was related to the horizontal (accommodation-induced) vergence component. Of course, no general conclusions can be drawn from just one patient, but the present findings suggest that it would be very interesting to determine both Listing's planes in a larger group of patients without effective binocular vision.

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